

Application No. 09/732,241
 Amendment Under 37 C.F.R. § 1.111 dated June 17, 2005
 Reply to Office Action of May 23, 2005

PATENT
 Attorney Docket No. P-095-US1
 Customer No. 27038

III. AMENDMENTS TO THE CLAIMS

This listing of the claims will replace all prior versions, and listings, of claims in the application.

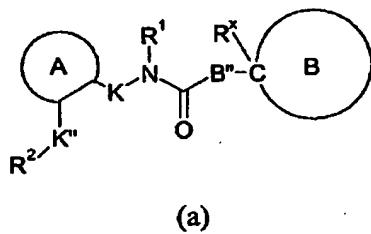
1. (Currently Amended) A compound of Formula (I):



(I)

wherein:

L_1 is a group of formula (a):



wherein:

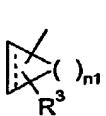
A is an aryl or a heteroaryl ring;

B'' is -O-;

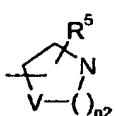
R^X is alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, acyl, acylamino, aminoacyloxy, aryl, carboxyalkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heteroaryl, heteroaralkyl, alkylsulfonyl, or alkylsulfinyl;

R^1 is hydrogen or alkyl;

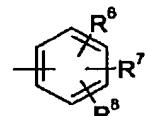
R^2 is Het, or is selected from [a] the group consisting of formula (i), (ii), and (iii):



(i)



(ii)



(iii)

wherein:

— is an optional double bond;

n_1 is an integer of from 1 to 4;

n_2 is an integer of from 1 to 3;

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V is -CH-, -O-, -S(O)_{n3}- -S(O)_{n3}- (where n₃ is an integer of from 0 to 2), or -NR⁴-
 (wherein R⁴ is hydrogen, alkyl, substituted alkyl, aryl, or heteroaryl);

"Het" is a heteroaryl ring which optionally attaches a the group of formula (a) to X a
linker;

R³ is hydrogen, alkyl, halo, amino, substituted amino, -OR^a (where R^a is hydrogen, alkyl,
 or acyl), or a covalent bond attaching a the group of formula (a) to X a-linker;

R⁵ is hydrogen, alkyl, halo, amino, substituted amino, -OR^b (where R^b is hydrogen or
 alkyl), aryl, aralkyl, heteroaralkyl, or a covalent bond attaching a the group of formula (a) to X a
linker;

R⁶, R⁷, and R⁸ are, independently of each other, hydrogen, halo, hydroxy hydroxyl,
 alkoxy, haloalkoxy, carboxy carboxyl, alkoxycarbonyl, alkyl optionally substituted with one, two
 or three substituents selected from halo, hydroxy hydroxyl, carboxy carboxyl, alkoxycarbonyl,
 alkylthio thioalkoxy, alkylsulfonyl, amino, substituted amino, or a covalent bond attaching a the
 group of formula (a) to X a-linker;

K is a bond or an alkylene group;

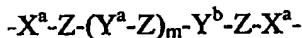
K" is a bond, -C(O)-, -S(O)_{n4}- (where n₄ is an integer of from 0 to 2), or an alkylene
 group optionally substituted with a hydroxyl group; and

B is heterocycloamino or heteroarylarnino, which optionally attaches a the group of
 formula (a) to X a-linker;

provided that at least one of the R³, R⁵, R⁶, R⁷, R⁸, "Het", heterocycloamino, or
 heteroarylarnino groups attaches a the group of formula (a) to X a-linker;

L₂ is an organic group comprising at least one primary, secondary or tertiary amine; and

X is a-linker of has the formula:



whercin

m is an integer of from 0 to 20;

X^a at each separate occurrence is selected from the group consisting of -O-, -S-, -NR-,
 -C(O)-, -C(O)O-, -C(O)NR-, -C(S)-, -C(S)O-, -C(S)NR- or a covalent bond where R is as
 defined below;

Z at each separate occurrence is selected from the group consisting of alkylene,
 substituted alkylene, cycloalkylene, substituted cycloalkylene, alkenylene, substituted

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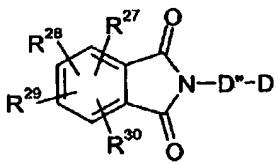
alkenylene, alkynylene, substituted alkynylene, cycloalkenylene, substituted cycloalkenylene, arylene, heteroarylene, heterocyclene, and a covalent bond; and

Y^a and Y^b at each separate occurrence are selected from the group consisting of -O-, -C(O)-, -OC(O)-, -C(O)O-, -NR-, -S(O)_n- S(O)_n-, -C(O)NR'-, -NR' C(O)-, -NR' C(O)NR'-, -NR'C(S)NR'-, -C(=NR')-NR'-, -NR'-C(=NR')-, -OC(O)-NR'-, -NR'-C(O)-O-, -P(O)(OR')-O-, -O-P(O)(OR')-, -S(O)_nCR'R''-, -S(O)_n-NR'-, -NR'-S(O)_n-, -S-S-, and a covalent bond; where n is 0, 1 or 2; and R, R' and R'' at each separate occurrence are selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkenyl, substituted alkenyl, cycloalkenyl, substituted cycloalkenyl, alkynyl, substituted alkynyl, aryl, heteroaryl and heterocyclic heterocycle; provided at least one of X^a , Y^a , Y^b or Z is not a covalent bond;

or a pharmaceutically acceptable salt; or prodrug thereof.

2. (Currently Amended) The compound of claim 1 wherein L₂ is a group selected from a the group consisting of:

(i) a group of formula (b):



(b)

wherein:

D'' is alkylene;

D is -NR³¹R³², -N<sup>+(R³³R³⁴R³⁵) or -OR³² where R³¹, R³³, and R³⁴ are, independently of each other, hydrogen, alkyl, or aralkyl; and R³² and R³⁵ represent a covalent bond attaching a the group of formula (b) to X a-linker;

R²⁷ is hydrogen, halo, nitro, cyano, hydroxy hydroxyl, alkoxy, carboxy carboxyl, alkoxy carbonyl, acyl, this thiol, alkylthio thioalkoxy, alkylsulfonyl, alkylsulfinyl, sulfonamido, alkylsulfonamido, carbamoyl, thiocarbamoyl, mono or dialkylcarbamoyl, amino, mono- or dialkylamino, aryl, aryloxy, arylthio, heteroaryl, heteroaryloxy heteroaryloxy, heteroarylthio thioheteroaryloxy, heterocyclic heterocycle, heterocyclyloxy heterocycloxy, aralkyl,

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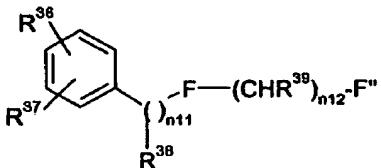
heteroaralkyl, or alkyl optionally substituted with one, two or three substituents selected from halo, hydroxy hydroxyl, carboxy carboxyl, alkoxy carbonyl, alkylthio thioalkoxy, alkylsulfonyl, amino, or substituted amino;

R^{28} is hydrogen, halo, nitro, cyano, hydroxy hydroxyl, alkoxy, carboxy carboxyl, alkoxy carbonyl, acyl, thio thiol, alkylthio thioalkoxy, alkylsulfonyl, alkylsulfinyl, sulfonamido, alkylsulfonamido, carbamoyl, thiocarbamoyl, mono or dialkylcarbamoyl, amino, mono- or dialkylamino, or alkyl optionally substituted with one, two, or three substituents selected from halo, hydroxy hydroxyl, carboxy carboxyl, alkoxy carbonyl, alkylthio thioalkoxy, alkylsulfonyl, amino, or substituted amino;

R^{29} and R^{30} are, independently of each other, hydrogen, alkyl, haloalkyl, halo, nitro, cyano, hydroxy hydroxyl, alkoxy, alkoxy carbonyl, acyl, thio thiol, alkylthio thioalkoxy, amino, mono- or dialkylamino; or

one of R^{27} , R^{28} , R^{29} , or R^{30} together with the adjacent group forms a methylenedioxy or ethylenedioxy group;

(ii) a group of formula (c):



(c)

wherein:

n_{11} is an integer of from 1 to 7;

n_{12} is 0 to 7;

F is $-NR^{40}-$, $-O-$, $-S-$, or $-CHR^{41}-$ (wherein R^{40} and R^{41} are, independently of each other, hydrogen, alkyl, or substituted alkyl);

F'' is a covalent bond, $-OR^{43}$, $-NR^{42}R^{43}$, or $-N^+R^{43}R^{44}R^{45}$ wherein R^{42} is hydrogen or alkyl, R^{44} and R^{45} are alkyl, and R^{43} is hydrogen, alkyl, or a covalent bond attaching a the group of formula (c) to X a-linker;

R^{36} is hydrogen, alkyl, halo, nitro, cyano, hydroxy hydroxyl, alkoxy, carboxy carboxyl, alkoxy carbonyl, acyl, thio thiol, alkylthio thioalkoxy, alkylsulfonyl, alkylsulfinyl, sulfonamido, alkylsulfonamido, carbamoyl, thiocarbamoyl, mono or dialkylcarbamoyl, amino, mono- or

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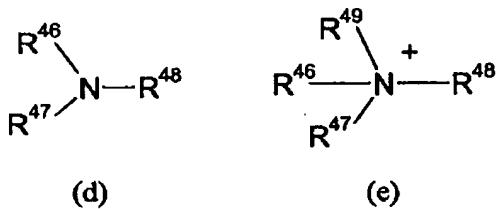
dialkylamino, aryl, aryloxy, arylthio, heteroaryl, heteraryloxy heteroaryloxy, heteroarylthio thioheteroaryloxy, heteroeyethyl heterocycle, heteroeyethyl oxy heterocyclooxy, aralkyl, heteroaralkyl, or alkyl optionally substituted with one, two or three substituents selected from halo, hydroxy hydroxyl, carboxy carboxyl, alkoxy carbonyl, alkylthio thioalkoxy, alkylsulfonyl, amino, or substituted amino;

R^{37} is hydrogen, alkyl, halo, nitro, cyano, hydroxy hydroxyl, alkoxy, alkoxy carbonyl, acyl, thio thiol, alkylthio thioalkoxy, amino, mono- or dialkylamino, aryl, aryloxy, arylthio, heteroaryl, heteraryloxy heteroaryloxy, heteroarylthio thioheteroaryloxy, heteroeyethyl heterocycle, heteroeyethyl oxy heterocyclooxy, aralkyl, heteroaralkyl, or alkyl optionally substituted with one, two or three substituents selected from halo, hydroxy hydroxyl, carboxy carboxyl, alkoxy carbonyl, alkylthio thioalkoxy, alkylsulfonyl, amino, or substituted amino; and

R^{38} is hydrogen, alkyl, halo, hydroxy hydroxyl, alkoxy, or a covalent bond attaching the ligand to X a-linker provided that at least one of R^{38} and R^{43} attaches a the group of formula (c) to X a-linker;

R^{39} is hydrogen, alkyl, halo, hydroxy hydroxyl, alkoxy, or substituted alkyl; and

(iii) a group of formula (d) or (e):



wherein:

R^{46} is alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, or heterocycle;

R^{47} is alkyl, substituted alkyl, aryl, acyl, heterocycle, or $-COOR^{50}$ where R^{50} is alkyl; or

R^{46} and R^{47} together with the nitrogen atom to which they are attached form a heterocycle, which heterocycle is optionally substituted with one or more alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, alkoxy, substituted alkoxy, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, acyl, acylamino, acyloxy, amino, substituted amino, aminoacyl, aminoacyloxy, oxyaminoacyl, azido, cyano, halogen halo, hydroxyl, keto, thionato, carboxyl, carboxylalkyl carboxylalkyl, thioaryloxy, thioheteroaryloxy, thioheterocyclooxy, thiol, thioalkoxy, substituted thioalkoxy, aryl, aryloxy, heteroaryl,

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heteroaryloxy, heterocyclic heterocycle, heterocyclooxy, hydroxyamino, alkoxyamino, nitro, -SO-alkyl, -SO-substituted alkyl, -SO-aryl, -SO-heteroaryl, -SO₂-alkyl, -SO₂-substituted alkyl, -SO₂-aryl or -SO₂-heteroaryl;

R⁴⁸ is a covalent bond that attaches a the group of formula (d) to X a-linker; and

R⁴⁹ is alkyl;

or a pharmaceutically acceptable salt; or prodrug thereof.

3. (Original) The compound of claim 1 or 2 wherein A is phenyl or pyridyl.
4. (Original) The compound of claim 1 or 2 wherein R¹ is hydrogen, methyl, or ethyl.
5. (Original) The compound of claim 1 or 2 wherein R² is pyrrolyl, pyridinyl, or imidazolyl.
6. (Original) The compound of claim 1 or 2 wherein R² is phenyl.
7. (Original) The compound of claim 1 or 2 wherein K is a bond or a methylene group.
8. (Original) The compound of claim 1 or 2 wherein K" is a bond.
9. (Original) The compound of claim 1 or 2 wherein R^x is alkyl, alkenyl, or alkynyl, each optionally substituted with 1 to 5 alkoxy or fluoro substituents.
10. (Currently Amended) The compound of claim 4 or 2 9 wherein R^x is (C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, each optionally substituted with 1 to 3 methoxy, ethoxy or fluoro substituents.
11. (Currently Amended) The compound of claim 4 or 2 9 wherein R^x is (C₁-C₆)alkyl, optionally substituted with 1 to 3 methoxy, ethoxy, or fluoro substituents.
12. (Original) The compound of claim 1 wherein R^x is methyl, ethyl, propyl, isopropyl,

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butyl, isobutyl or secbutyl, optionally substituted with methoxy or ethoxy or with 1 to 3 or fluoro substituents.

13. (Original) The compound of claim 1 wherein R^x is methyl, ethyl, methoxymethyl, ethoxymethyl, methoxyethyl, ethoxyethyl, fluoromethyl, difluoromethyl trifluoromethyl, trifluoromethoxymethyl, formyl, or acetyl.

14. (Original) The compound of claim 1 or 2 wherein R^x is methyl, ethyl, methoxymethyl, fluoromethyl, difluoromethyl, or trifluoromethyl.

15. (Currently Amended) The compound of claim 1 or 2 wherein B is a heterocycloamino group which attaches a the group of formula (a) to X a-linker.

16. (Currently Amended) The compound of claim 1-~~or~~-2 15 wherein B is pyrrolidine, piperidine, or hexahydroazepine attaching a the group of formula (a) to X a-linker.

17. (Currently Amended) The compound of claim 1-~~or~~-2 16 wherein B is piperidine wherein the nitrogen atom of said piperidine attaches a the group of formula (a) to X a-linker.

18. (Currently Amended) The compound of claim 1-~~or~~-2 16 wherein B is piperidin-3-yl or piperidin-4-yl wherein the nitrogen at the 1 position optionally attaches a the group of formula (a) to X a-linker.

19. (Original) The compound of claim 1 wherein B taken together with R^x is 4-methylpiperidine-1,4-diyl.

20. (Original) The compound of claim 2 wherein L₂ is a group of formula (d) or (e).

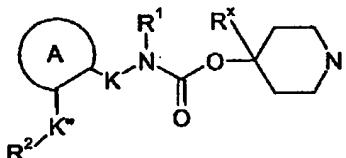
21. (Previously Presented) The compound of claim 20 wherein: R⁴⁶ is alkyl or substituted alkyl; R⁴⁷ is alkyl, substituted alkyl, or heterocycle; or R⁴⁶ and R⁴⁷ together with the nitrogen atom to which they are attached form a heterocycle.

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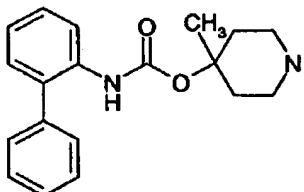
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22. Canceled.

23. (Original) The compound of claim 1 or 2 wherein L₁ is:



24. (Original) The compound of claim 23 wherein L₁ is:



25. (Currently Amended) The compound of claim 24 wherein the piperidino nitrogen of L₁ is bonded attached to X.

26. (Previously Presented) The compound of claim 1 or 2 wherein X is alkylene optionally substituted with one, two, or three hydroxy groups, alkylene wherein one, two, or three carbon atoms have been replaced by an oxygen atom, or an -alkylene-phenylene-alkylene- wherein the phenylene ring is optionally substituted with one or two chloro or fluoro groups.

27. Canceled.

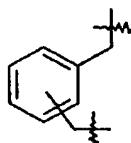
28. (Currently Amended) The compound of claim 1 or 2 wherein X is an alkylene group having from 3 to 20 carbon atoms; wherein one or more carbon atoms in the alkylene group is optionally replaced with -O-; and wherein the chain is optionally substituted on carbon with one or more hydroxyl groups.

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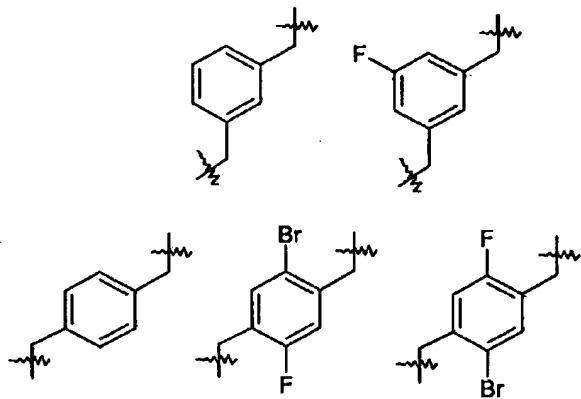
29. (Original) The compound of claim 1 or 2 wherein X is nonane-1,9-diyl, octane-1,8-diyl, propane-1,3-diyl, 2-hydroxypropane-1,3-diyl, or 5-oxa-nonane-1,9-diyl.

30. (Currently Amended) The compound of claim 1 or 2 wherein X has the following formula:

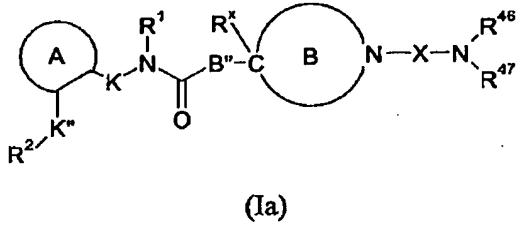


wherein the phenyl ring is optionally substituted with 1, 2, or 3 fluoro groups.

31. (Previously Presented) The compound of claim 1 or 2 wherein X has one of the following formulas:



32. (Currently Amended) The compound of claim 2 which is a compound of having Formula (Ia):



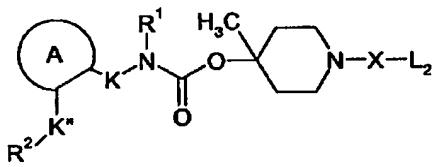
or a pharmaceutically acceptable salt or prodrug thereof.

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33. Canceled.

34. (Currently Amended) The compound of claim 1 which is a compound of formula having Formula (III):



(III)

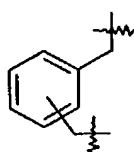
wherein R², K⁺, A, K, R¹, X, and L₂ have the values defined in claim 1; or a pharmaceutically acceptable salt or prodrug thereof.

35. Canceled.

36. (Currently Amended) The compound of claim 34 wherein X is an alkylene group having from 3 to 20 carbon atoms; wherein one or more carbon atoms in the alkylene group is optionally replaced with -O-; and wherein the chain is optionally substituted on carbon with one or more hydroxyl groups.

37. (Original) The compound of claim 34 wherein X is nonane-1,9-diyl, octane-1,8-diyl, propane-1,3-diyl, 2-hydroxypropane-1,3-diyl, or 5-oxa-nonane-1,9-diyl.

38. (Original) The compound of claim 34 wherein X has the following formula:

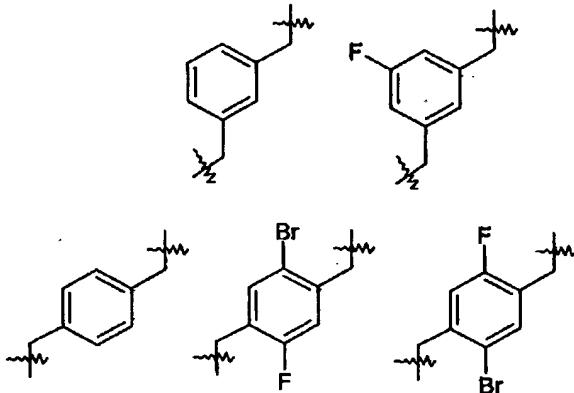


wherein the phenyl ring is optionally substituted with 1, 2, or 3 fluoro groups.

39. (Previously Presented) The compound of claim 34 wherein X has one of the following formulas:

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40. (Currently Amended) The compound of claim 2 20 wherein L₂ is a group of formula (d) wherein R⁴⁶ is a heterocycle, optionally substituted with 1 to 5 substituents independently selected from the group consisting of alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, and substituted alkynyl; and R⁴⁷ is alkyl, substituted alkyl, acyl, or -COOR⁵⁰.

41. (Currently amended) The compound of claim 2 20 wherein L₂ is a group of formula (d) wherein R⁴⁶ is alkyl that is optionally substituted with from 1 to 5 substituents independently selected from the group consisting of alkoxy, substituted alkoxy, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, acyl, acylamino, acyloxy, amino, aminoacyl, aminoacyloxy, oxyaminoacyl, cyano, halogen halo, hydroxyl, keto, thioketo, carboxylalkyl carboxyalkyl, thioaryloxy, thioheteroaryloxy, thioheterocyclooxy, thiol, thioalkoxy, substituted thioalkoxy, heterocyclic heterocycle, heterocyclooxy, hydroxyamino, alkoxyamino, and NR^aR^b, wherein R^a and R^b may be the same or different [and] and are chosen from hydrogen, alkyl, substituted alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, and heterocyclic heterocycle.

42. (Currently amended) The compound of claim 2 20 wherein L₂ is a group of formula (d) wherein R⁴⁶ is 3-piperidinyl, 4-piperidinyl, or 3-pyrrolidinyl, which R⁴⁶ is optionally substituted with 1 to 3 substituents independently selected from the group consisting of alkoxy, substituted alkoxy, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, acyl, acylamino, acyloxy, amino, substituted amino, aminoacyl, aminoacyloxy, oxyaminoacyl, cyano, halogen halo, hydroxyl, keto, thioketo, carboxylalkyl carboxyalkyl, thioaryloxy,

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thioheteroaryloxy, thioheterocyclooxy, thiol, thioalkoxy, substituted thioalkoxy, heterocyclic heterocycle, heterocyclooxy, hydroxyamino, alkoxyamino, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, and substituted alkynyl.

43. (Currently amended) The compound of claim 2 20 wherein R⁴⁶ and R⁴⁷ together with the nitrogen atom to which they are attached form a piperidine or pyrrolidine ring which ring is optionally substituted with 1 to 3 substituents independently selected from the group consisting of alkoxy, substituted alkoxy, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, acyl, acylamino, acyloxy, amino, substituted amino, aminoacyl, aminoacyloxy, oxyaminoacyl, cyano, halogen halo, hydroxyl, keto, thioketo, carboxylalkyl carboxyalkyl, thioaryloxy, thioheteroaryloxy, thioheterocyclooxy, thiol, thioalkoxy, substituted thioalkoxy, heterocyclic heterocycle, heterocyclooxy, hydroxyamino, alkoxyamino, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, and substituted alkynyl.

44. (Currently amended) The compound of claim 2 20 wherein R⁴⁶ and R⁴⁷ together with the nitrogen atom to which they are attached form a heterocycle that is an aza-crown ether.

45. (Original) The compound of claim 44 wherein the aza-crown ether is 1-aza-12-crown-4, 1-aza-15-crown-5, or 1-aza-18-crown-6.

46. Canceled.

47. (Previously Presented) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of claim 1 or 2.

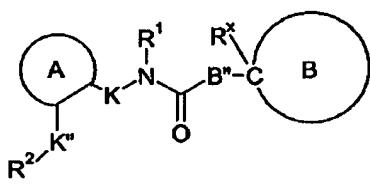
48. Canceled.

49. Canceled.

50. (Currently Amended) A compound of formula L₁-H wherein L₁ has the values defined in claim 1; is a group of formula (a):

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(a)

wherein:

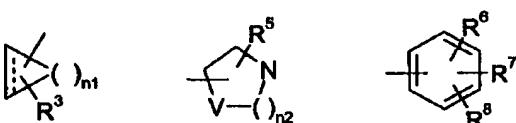
A is an aryl or a heteroaryl ring;

B'' is -O-;

R³ is alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, acyl, acylamino, aminoacyloxy, aryl, carboxyalkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substitutes cycloalkenyl, heteroaryl, heteroaralkyl, alkylsulfonyl, or alkylsulfinyl;

R¹ is hydrogen or alkyl;

R² is Het, or is selected from the group consisting of formula (i), (ii), and (iii):



(i)

(ii)

(iii)

wherein:

---- is an optional double bond;

n₁ is an integer of from 1 to 4;

n₂ is an integer of from 1 to 3;

V is -CH-, -O-, -S(O)_{n₃}- (where n₃ is an integer of from 0 to 2), or -NR⁴- (wherein R⁴ is hydrogen, alkyl, substituted alkyl, aryl, or heteroaryl);

"Het" is a heteroaryl ring which optionally attaches the group of formula (a) to the hydrogen in L₁-H;

R³ is hydrogen, alkyl, halo, amino, substituted amino, -OR^a (where R^a is hydrogen, alkyl, or acyl), or a covalent bond attaching the group of formula (a) to the hydrogen in L₁-H;

R⁵ is hydrogen, alkyl, halo, amino, substituted amino, -OR^b (where R^b is hydrogen or alkyl), aryl, aralkyl, heteroaralkyl, or a covalent bond attaching the group of formula (a) to the hydrogen in L₁-H;

R⁶, R⁷, and R⁸ are, independently of each other, hydrogen, halo, hydroxyl, alkoxy,

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haloalkoxy, carboxyl, alkoxy carbonyl, alkyl optionally substituted with one, two or three substituents selected from halo, hydroxyl, carboxyl, alkoxy carbonyl, thioalkoxy, alkylsulfonyl, amino, substituted amino, or a covalent bond attaching the group of formula (a) to the hydrogen in L₁-H;

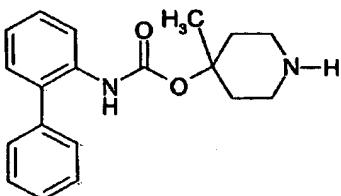
K is a bond or an alkylene group;

K" is a bond, -C(O)-, -S(O)_{n4}- (where n₄ is an integer of from 0 to 2), or an alkylene group optionally substituted with a hydroxyl group; and

B is heterocycloamino or heteroaryl amino, which optionally attaches the group of formula (a) to the hydrogen in L₁-H;

provided that at least one of the R³, R⁵, R⁶, R⁷, R⁸, "Het", heterocycloamino, or heteroaryl amino groups attaches the group of formula (a) to the hydrogen in L₁-H; or a salt thereof.

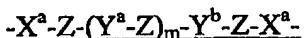
51. (Currently Amended) The compound of claim 50 which is a compound of having formula (V):



(V)

or a salt thereof.

52. (Currently Amended) A compound of formula R_a-X-L₂ wherein X and has the formula:



wherein

m is an integer of from 0 to 20;

X^a at each separate occurrence is selected from the group consisting of -O-, -S-, -NR-, -C(O)-, -C(O)O-, -C(O)NR-, -C(S)-, -C(S)O-, -C(S)NR- or a covalent bond;

Z at each separate occurrence is selected from the group consisting of alkylene, substituted alkylene, cycloalkylene, substituted cycloalkylene, alkenylene, substituted

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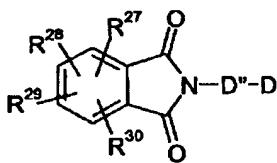
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alkenylene, alkynylene, substituted alkynylene, cycloalkenylene, substituted cycloalkenylene, arylene, heteroarylene, heterocyclene, and a covalent bond; and

Y^a and Y^b at each separate occurrence are selected from the group consisting of -O-, -C(O)-, -OC(O)-, -C(O)O-, -NR-, -S(O)_n-, -C(O)NR'-, -NR' C(O)-, -NR' C(O)NR'-, -NR' C(S)NR'-, -C(=NR')-NR'-, -NR'-C(=NR')-, -OC(O)-NR'-, -NR'-C(O)-O-, -P(O)(OR')-O-, -O-P(O)(OR')-, -S(O)_nCR'R''-, -S(O)_n-NR'-, -NR'-S(O)_n-, -S-S-, and a covalent bond; where n is 0, 1 or 2; and R, R' and R'' at each separate occurrence are selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkenyl, substituted alkenyl, cycloalkenyl, substituted cycloalkenyl, alkynyl, substituted alkynyl, aryl, heteroaryl and heterocycle; provided at least one of X^a, Y^a, Y^b or Z is not a covalent bond;

L₂ have the values defined in claim 2; is selected from the group consisting of:

(i) a group of formula (b):



(b)

wherein:

D'' is alkylene;

D is -NR³¹R³², -N⁺(R³³R³⁴R³⁵) or -OR³² where R³¹, R³³, and R³⁴ are, independently of each other, hydrogen, alkyl, or aralkyl; and R³² and R³⁵ represent a covalent bond attaching the group of formula (b) to X;

R²⁷ is hydrogen, halo, nitro, cyano, hydroxyl, alkoxy, carboxyl, alkoxy carbonyl, acyl, thiol, thioalkoxy, alkylsulfonyl, alkylsulfinyl, sulfonamido, alkylsulfonamido, carbamoyl, thiocarbamoyl, mono or dialkylcarbamoyl, amino, mono- or dialkylamino, aryl, aryloxy, arylthio, heteroaryl, heteroaryloxy, thioheteroaryloxy, heterocycle, heterocycloxy, aralkyl, heteroaralkyl, or alkyl optionally substituted with one, two or three substituents selected from halo, hydroxyl, carboxyl, alkoxy carbonyl, thioalkoxy, alkylsulfonyl, amino, or substituted amino;

R²⁸ is hydrogen, halo, nitro, cyano, hydroxyl, alkoxy, carboxyl, alkoxy carbonyl, acyl, thiol, thioalkoxy, alkylsulfonyl, alkylsulfinyl, sulfonamido, alkylsulfonamido, carbamoyl,

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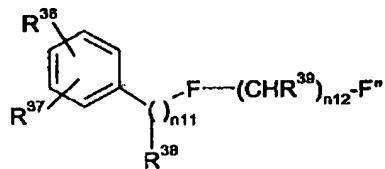
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thiocarbamoyl, mono or dialkylcarbamoyl, amino, mono- or dialkylamino, or alkyl optionally substituted with one, two, or three substituents selected from halo, hydroxyl, carboxyl, alkoxy carbonyl, thioalkoxy, alkylsulfonyl, amino, or substituted amino;

R²⁹ and R³⁰ are, independently of each other, hydrogen, alkyl, haloalkyl, halo, nitro, cyano, hydroxyl, alkoxy, alkoxy carbonyl, acyl, thiol, thioalkoxy, amino, mono- or dialkylamino; or

one of R²⁷, R²⁸, R²⁹, or R³⁰ together with the adjacent group forms a methylenedioxy or ethylenedioxy group;

(ii) a group of formula (c):



(c)

wherein:

n₁₁ is an integer of from 1 to 7;

n₁₂ is 0 to 7;

F is -NR⁴⁰- , -O-, -S-, or -CHR⁴¹- (wherein R⁴⁰ and R⁴¹ are, independently of each other, hydrogen, alkyl, or substituted alkyl);

F" is a covalent bond, -OR⁴³, -NR⁴²R⁴³, or -N⁺R⁴³R⁴⁴R⁴⁵ wherein R⁴² is hydrogen or alkyl, R⁴⁴ and R⁴⁵ are alkyl, and R⁴³ is hydrogen, alkyl, or a covalent bond attaching the group of formula (c) to X;

R³⁶ is hydrogen, alkyl, halo, nitro, cyano, hydroxyl, alkoxy, carboxyl, alkoxy carbonyl, acyl, thiol, thioalkoxy, alkylsulfonyl, alkylsulfinyl, sulfonamido, alkylsulfonamido, carbamoyl, thiocarbamoyl, mono or dialkylcarbamoyl, amino, mono- or dialkylamino, aryl, aryloxy, arylthio, heteroaryl, heteroaryloxy, thioheteroaryloxy, heterocycle, heterocycloxy, aralkyl, heteroaralkyl, or alkyl optionally substituted with one, two or three substituents selected from halo, hydroxyl, carboxyl, alkoxy carbonyl, thioalkoxy, alkylsulfonyl, amino, or substituted amino;

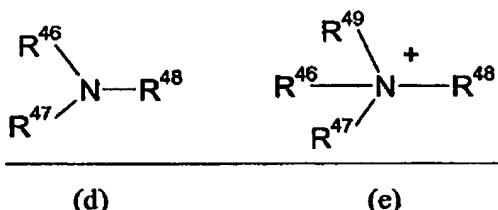
R³⁷ is hydrogen, alkyl, halo, nitro, cyano, hydroxyl, alkoxy, alkoxy carbonyl, acyl, thiol, thioalkoxy, amino, mono- or dialkylamino, aryl, aryloxy, arylthio, heteroaryl, heteroaryloxy,

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thioheteroaryloxy, heterocycle, heterocyclooxy, aralkyl, heteroaralkyl, or alkyl optionally substituted with one, two or three substituents selected from halo, hydroxyl, carboxyl, alkoxy carbonyl, thioalkoxy, alkylsulfonyl, amino, or substituted amino; and
R³⁸ is hydrogen, alkyl, halo, hydroxyl, alkoxy, or a covalent bond attaching the ligand to X provided that at least one of R³⁸ and R⁴³ attaches the group of formula (c) to X;
R³⁹ is hydrogen, alkyl, halo, hydroxyl, alkoxy, or substituted alkyl; and

(iii) a group of formula (d) or (e):



wherein:

R⁴⁶ is alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, or heterocycle;
R⁴⁷ is alkyl, substituted alkyl, aryl, acyl, heterocycle, or -COOR⁵⁰ where R⁵⁰ is alkyl; or
R⁴⁶ and R⁴⁷ together with the nitrogen atom to which they are attached form a heterocycle, which heterocycle is optionally substituted with one or more alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, alkoxy, substituted alkoxy, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, acyl, acylamino, acyloxy, amino, substituted amino, aminoacyl, aminoacyloxy, oxyaminoacyl, azido, cyano, halo, hydroxyl, keto, thioketo, carboxyl, carboxyalkyl, thioaryloxy, thioheteroaryloxy, thioheterocyclooxy, thiol, thioalkoxy, substituted thioalkoxy, aryl, aryloxy, heteroaryl, heteroaryloxy, heterocycle, heterocyclooxy, hydroxyamino, alkoxyamino, nitro, -SO-alkyl, -SO-substituted alkyl, -SO-aryl, -SO-heteroaryl, -SO₂-alkyl, -SO₂-substituted alkyl, -SO₂-aryl or -SO₂-heteroaryl;

R⁴⁸ is a covalent bond that attaches the group of formula (d) to X; and

R⁴⁹ is alkyl; and

R_a is a suitable leaving group.